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NELSON MULLINS RILEY & SCARBOROUGH LLP
FLOOR 30, SUITE 3000
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
SCHWADRON, RONALD B	
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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte RALPH M. STEINMAN, MICHEL C. NUSSENZWEIG, WILLIAM J. SWIGGARD, and WANPING JIANG

Appeal 2011-012057
Application 09/586,704
Technology Center 1600

Before DEMETRA J. MILLS, ERIC GRIMES, and ERICA A. FRANKLIN, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to vaccines. The Patent Examiner rejected the claims as failing to comply with the written description requirement and as lacking enablement. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

STATEMENT OF THE CASE

Claims 26-28, 35, 36, 38-40, and 42-43 are on appeal. Independent claims 26, 35, 36, and 40 are representative and read as follows:

26. A vaccine for inducing an immune response comprising an antigen conjugated to an anti-human Dendritic and Epithelial Cell 205 (DEC-205) antibody or an anti-murine DEC-205 antibody reactive with a human DEC-205 protein, said human DEC-205 protein comprising an amino acid sequence as set forth in SEQ ID NO: l.

35. A vaccine for inducing an immune response comprising an antigen conjugated to an anti-human Dendritic and Epithelial Cell 205 (DEC-205) antibody, wherein the antibody is reactive with the amino acid sequence as set forth in SEQ ID NO: 1.

36. A vaccine for inducing an immune response comprising an antigen conjugated to an anti-mouse Dendritic and Epithelial Cell-205 (DEC-205) antibody, wherein the antibody is reactive with the amino acid sequence as set forth in SEQ ID NO: 1.

40. A vaccine for inducing an immune response comprising an antigen conjugated to an antibody which binds mouse Dendritic and Epithelial Cell 205 (DEC-205) having the amino acid sequence of SEQ ID NO: 3, wherein the antibody cross reacts with human DEC-205.

The Examiner rejected the claims as follows:

- claims 26-28, 35, 36, 38-40, 42, and 43 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement;
- claims 26-28, 35, 36, 38, and 39 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (new matter); and
- claims 26-28, 35, 36, 38-40, 42, and 43 under 35 U.S.C. § 112, first paragraph, as lacking enablement.

WRITTEN DESCRIPTION

The Examiner's position is that the Specification does not convey to an artisan that the Applicant had possession, at the time of filing, of the

conjugate recited in the claimed composition. (Ans. 5.) The Examiner found that the claim term "[']human DEC-205[']' would appear to encompass full length human DEC-205[,] as well as mutants and variants or alleles of said human protein…." (*Id.* at 5-6.) The Examiner found that while the full length murine DEC-205 protein was disclosed in the Specification of the parent application, there was no disclosure of the full length human DEC-205. (*Id.* at 6.) Specifically, the Examiner found that human DEC-205 contains approximately 1800 amino acids and that the Specification disclosed sequences for two peptides derived from the human DEC-205 having 30 and 25 amino acids, respectively, but did not disclose the identity of the remaining approximately 1750 amino acids. (*Id.*)

Regarding claims 35, 36, 38, and 39, the Examiner stated that the "claims recite the use of an antihuman DEC 205 antibody which binds an amino acid sequence 'as set forth' in SEQ. ID. No. 1 and wherein said language is interpreted as equivalent in scope to comprising." (*Id.* at 6.) According to the Examiner, the claim therefore "could be interpreted as encompassing antibodies which bound the sequence comprising said amino acid sequence wherein said sequence would encompass full length human DEC-205." (*Id.*)

Regarding claim 40, the Examiner found that in the absence of human DEC-205, it would not be possible to establish which antibodies reacted with human DEC-205. (*Id.*)

Appellants contend, regarding claims 26-28, that the Specification's "disclosure of the partial human DEC-205 sequence and the full length murine DEC-205 sequence, in combination with knowledge available in the art, are sufficient to demonstrate to one of ordinary skill that Applicants had

possession of the claimed invention, *i.e.*, an antibody vaccine conjugate directed to human DEC-205 protein, at the time the present application was filed." (App. Br. 7.)

According to Appellants, the fact that they successfully isolated and characterized full-length mouse DEC-205 from whole murine thymus using mAb NLDC-145, an anti-mouse DEC-205 antibody, and successfully raised antibodies against N-terminal peptides from mouse DEC-205 protein "provides ***clear evidence*** that the partial human DEC-205 sequence described in the present disclosure put Appellants in possession of the complete DEC-205 protein and antibodies against the protein." (*Id.*) Further, Appellants assert that "[i]t was also well within the skill in the art to have generated full-length human DEC-205 protein, as well as variants of the human DEC-205 protein." (*Id.*)

Additionally, Appellants submit the Declaration of Dr. Michel Nussenzweig as evidence that "the cloning techniques and techniques for generating antibodies described in the specification were ultimately successfully used to clone and isolate human DEC-205, and to produce antibodies against full-length human DEC-205." (*Id.* at 11.) According to Appellants, this fact "provides clear evidence that Appellants were in fact indeed in possession of the claimed invention based on the descriptive text provided within the four corners of Appellants' originally filed disclosure." (*Id.*)

Moreover, Appellants contend that "the structure and function of human DEC-205 clearly correlates to that of mouse DEC-205," such that the disclosure of an "in-depth characterization of mouse DEC-205, including its

full-length sequence… provides further descriptive basis for fully meeting the Written Description requirement." (*Id.* at 8-9.)

Regarding claims 35, 36, 38 and 39, Appellants assert that these claims "are drawn to antibody conjugates which do, indeed, bind to a particular epitope of human DEC-205, namely the C-terminal sequence (SEQ ID NO:1)." (*Id.* at 6.)

Regarding claims 40, 42 and 43, Appellants assert that "these claims are drawn to a vaccine comprising an antigen conjugated to an antibody that binds to *full length murine DEC-205 protein* (SEQ ID NO:3)," which sequence is explicitly disclosed in the Specification. (*Id.*) Further, Appellants assert that while these claims require the antibody conjugates to "cross-react with human DEC-205, the epitopes of human DEC-205 that the conjugates bind to are by definition, shared with (*i.e.*, cross-reactive with) murine DEC-205." (*Id.* at 7.) According to Appellants, "these epitopes are inherently provided as part of the full length murine DEC-205 sequence recited in the claims (SEQ ID NO: 3)." (*Id.*)

Analysis

I. Claims 26-28

After considering all the evidence and arguments, we conclude that the disclosure as originally filed did not reasonably convey to those skilled in the art that the inventors had possession of the subject matter of claims 26-28 as of the filing date. *Ariad Pharm., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed Cir. 2010). These claims are directed to a vaccine comprising an antigen conjugated to an anti-human DEC-205 antibody or an anti-murine DEC-205 antibody reactive with a human DEC-205 protein, said human DEC-205 protein comprising an amino acid sequence as set

forth in SEQ ID NO: 1. Appellants do not challenge the Examiner's interpretation of the claim as encompassing antibody conjugates that bind any part of full length human DEC-205, as well as variants thereof. Nor do Appellants dispute the Examiner's finding that the full length human DEC-205 was not disclosed in the Specification. Rather, Appellants assert that the inventors, nevertheless, had full possession of the complete human DEC-205 protein, and antibody conjugates against the protein, at the time the application was filed, as evidenced by the disclosure of the partial human DEC-205 sequences, the full length murine DEC-205 sequence, and the skill and knowledge available in the art to generate full-length human DEC-205 and its variants. (App. Br. 7.) According to Appellants, Dr. Nussenzweig's declaratory testimony that "the cloning techniques and techniques for generating antibodies described in the specification were ultimately successfully used to clone and isolate human DEC-205, and to produce antibodies against full-length human DEC-205" also provides evidence that the inventors were in possession of the claimed invention. (*Id.* at 11.)

We disagree with Appellants. Dr. Nussenzweig's declaration is directed to Application No. 09/925,284, a Continuation-in-Part application of the present application, and having a filing date of August 9, 2001. (Dec. ¶ 3.) As the Examiner correctly explained, the cloned human DEC-205 sequence referred to by Dr. Nussenzweig was not disclosed in the instant Specification. Moreover, the fact that Dr. Nussenzweig "ultimately successfully" cloned and isolated human DEC-205 and produced antibodies against full length human DEC-205 does not establish that the inventors were in possession of the subject matter at the time the instant application was filed. Consequently, while we recognize Dr. Nussenzweig's apparent

expertise in the field of immunology, we do not accord his declaration persuasive weight. The written description requirement "requires a description of an invention, not an indication of a result that one might achieve if one made that invention." *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1568 (Fed. Cir. 1997). Indeed, to comply with the written description requirement, an applicant must "describe[] the invention, with all its claimed limitations, not that which makes it obvious…." *Id.* at 1566 (citation omitted). Accordingly, we affirm the rejection of claims 26-28.

II. Claims 35, 36, 38, and 39

Claims 35, 36, 38 and 39 are directed to a vaccine comprising an antigen conjugated to a DEC-205 antibody, wherein the antibody is reactive with the specifically disclosed amino acid sequence, i.e., as set forth in SEQ ID NO: 1. The Examiner has not provided a persuasive basis for construing claims 35, 36, 38 and 39 to encompass antibody conjugates that bind to parts of DEC-205 other than SEQ ID NO: 1. We agree with Appellants that the disclosure of SEQ ID NO: 1 provides evidence that the inventors had possession of this claimed subject matter as of the filing date.

Accordingly, we reverse the rejection of claims 35, 36, 38 and 39.

III. Claims 40, 42, and 43

Claims 40, 42, and 43 are directed to a vaccine comprising an antigen to an antibody which binds mouse DEC-205 having the amino acid sequence of SEQ ID NO:3, wherein the antibody cross reacts with human DEC-205. While we agree with Appellants that the full length murine DEC-205 protein is explicitly disclosed in the Specification as SEQ ID NO:3, we do not agree that this disclosure provides evidence that the inventors were in possession

of the recited antibody conjugates, *wherein the antibody cross reacts with human DEC-205*. Specifically, Appellants have not provided evidence establishing such possession by merely asserting that "the epitopes of human DEC-205 that the conjugates bind to are …, by definition, shared with (*i.e.*, cross-reactive with) murine DEC-205." (App. Br. 7.) Appellants have not described which epitopes of murine DEC-205 are shared with (i.e., cross-reactive with) those of human DEC-205, and therefore have not adequately shown that they were in possession of antibody conjugates binding to such epitopes at the time the application was filed.

Accordingly, we affirm the rejection of claims 40, 42, and 43.

NEW MATTER

The Examiner rejected claims 26-28, 35, 36, 38, and 39 as containing new matter. (Ans. 8.) We do not reach the new matter rejection of claims 26-28, as we have previously affirmed the Examiner's rejection of these claims as failing to comply with the written description requirement.

Regarding claims 35, 36, 38, and 39, the Examiner relies on the same findings raised regarding the first rejection of the claims as failing to comply with the written description requirement. (*See* Ans. 8-9.) Therefore, we reverse the rejection for the same reasons discussed regarding the first rejection of the claims as failing to comply with the written description requirement.

ENABLEMENT

The Examiner's position is that the Specification is not enabling for the claimed vaccine. (Ans. 9.) The Examiner found that the Specification does not disclose how to use the instant invention for the in vivo treatment

or prevention of disease in humans. (*Id.*) The Examiner found the state of the art is unpredictable in the absence of evidence as to how to use the invention. (*Id.* at 9-10.) In particular, the Examiner found that Schjetne[1] disclosed that DEC-205 antigen conjugates administered in vivo require CD40 ligation in vivo to induce an immune response. (*Id.* at 11.) Therefore, the Examiner found that a skilled artisan would not expect the claimed invention to induce an immune response because it lacks an agent that causes CD40 ligation. (*Id.* at 12.) Further, the Examiner found that Schjetne disclosed that even in the presence of CD40 ligation, tumor vaccines would be unsuitable for treating tumor bearing animals. (*Id.*)

Additionally, regarding claims 27, 29, and 43, the Examiner found that there is currently no known tumor vaccine that can be used to treat cancer in humans where the vaccine uses tumor antigens. (*Id.*) The Examiner also found that there is no disclosure in the Specification of any in vivo evidence in any model wherein the claimed invention is used as a vaccine. (*Id.*) Therefore, while finding that the skill in the art is high, the Examiner concluded that undue experimentation would be required for a skilled artisan to practice the claimed invention. (*Id.*)

Appellants contend that the Specification "does indeed provide sufficient teachings, when combined with the knowledge in the art at the time the present application was filed, for one of ordinary skill to have made and used the claimed conjugates without undue experimentation, ***as well as***

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[1] Karoline W. Schjetne et al., *Delivery of Antigent to CD40 Induces Protective Immune Responses against Tumors*, 178 J. IMMUNOLOGY, 4169-4176 (2007).

working data which would provide … a more than reasonable basis for accepting that the disclosure is enabling for in vitro and in vivo uses." (App. Br. 14.) Specifically, Appellants assert that the Specification provides examples demonstrating (a) *in vitro* that DEC-205 receptors are internalized after being bound by anti-DEC-205 antibodies, and (b) successful presentation of rabbit IgG-peptide/MHC complexes to T cell clones using rabbit-anti-DEC-205 antibodies. (*Id.*) Appellants also make reference to "post-filing *in vivo* working examples" as further evidence that the claims are fully enabled for *in vivo* vaccine therapy. (*Id.*) Moreover, Appellants assert that the claims are drawn to vaccine conjugates and not to specific *in vivo* uses, thus, the claims satisfy the enablement requirement by being "enabled for *in vitro* uses, notwithstanding in vivo uses." (*Id.* at 15.)

Regarding Schjetne, Appellants assert that, contrary to the Examiner's suggestion, the reference does not support a lack of predictability for the presently claimed vaccine conjugates targeted to DEC-205. (*Id.* at 16.) According to Appellants, Schjetne disclosed that DEC-205 is an efficient endocytic receptor expressed on dendritic cells and that the "**linkage between the CD40-targeting unit and the Ag might only be required if the Ag is otherwise inefficiently endocytosed by APC, as was the case in the design of the present study**." (*Id.*)(quoting Schjetne at 4175).

After considering the arguments and evidence, we agree with Appellants that the evidence of record supports enablement. The Examiner found that a skilled artisan would have had to resort to undue experimentation to use the claimed invention for in vivo treatment or prevention of disease in humans. (Ans. 9.) However, the rejected claims are not directed to a method of in vivo treatment or prevention of disease in

humans, but rather to vaccines for inducing an immune response. Thus, we agree with Appellants that the claims are not drawn to specific *in vivo* uses, and satisfy the enablement requirement by being "enabled for *in vitro* uses…." (App. Br. 15.) *See Johns Hopkins Univ. v. Cellpro, Inc.,* 152 F.3d 1342, 1361 (Fed. Cir. 1998) (quoting *Engel Indus., Inc. v. Lockformer Co.,* 946 F.2d 1528, 1533 (Fed. Cir. 1991)("The enablement requirement is met if the description enables any mode of making and using the invention.")).

Accordingly, we reverse the non-enablement rejection.

SUMMARY

We affirm the rejection of claims 26-28, 39, 40, 42, and 43 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement;

we reverse the rejection of claims 35, 36, and 38 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement;

we reverse the rejection of claims 35, 36, and 38 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (new matter).

we reverse the rejection of claims 26-28, 35, 36, 38-40, 42, and 43 under 35 U.S.C. § 112, first paragraph, as lacking enablement.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

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